



General

Guideline Title

ACR Appropriateness Criteria® renal transplant dysfunction.

Bibliographic Source(s)

Taffel MT, Nikolaidis P, Beland MD, Blaufox MD, Dogra VS, Goldfarb S, Gore JL, Harvin HJ, Heilbrun ME, Heller MT, Khatri G, Preminger GM, Purysko AS, Smith AD, Wang ZJ, Weinfeld RM, Wong-You-Cheong JJ, Remer EM, Lockhart ME, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® renal transplant dysfunction. Reston (VA): American College of Radiology (ACR); 2016. 12 p. [90 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dighe M, Remer E, Casalino D, Bishoff JT, Blaufox MD, Coursey CA, Eberhardt SC, Goldfarb S, Harvin HJ, Lazarus E, Leyendecker JR, Lockhart ME, Nikolaidis P, Oto A, Porter C, Sheth S, Vikram R, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® renal transplant dysfunction. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 7 p. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Renal Transplant Dysfunction

Variant 1: Renal transplant dysfunction.

Radiologic Procedure	Rating	Comments	RRL*
US duplex Doppler kidney transplant	9	This procedure is a first-line imaging evaluation.	O
Tc-99m MAG3 scan kidney	7	This procedure is complementary to US duplex Doppler.	☼☼☼
Tc-99m DTPA scan kidney	5		☼☼☼
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			Relative Radiation Level

Radiologic Procedure	Rating	Comments	RRI*
Arteriography kidney		This procedure is used after noninvasive vascular assessment has been performed. It is used to confirm RAS or other vascular abnormality and guide treatment.	
CTA abdomen and pelvis IV with contrast	5		☢☢☢☢☢
CT abdomen and pelvis without and with IV contrast	4		☢☢☢☢
CT abdomen and pelvis without IV contrast	4		☢☢☢☢
MRI abdomen and pelvis without and with IV contrast	4		O
MRI abdomen and pelvis without IV contrast	4		O
MRA abdomen and pelvis without and with IV contrast	4		O
MRA abdomen and pelvis without IV contrast	4		O
X-ray intravenous urography	1		☢☢☢
X-ray antegrade pyelography	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Renal transplantation is the preferred treatment method in patients with end-stage renal failure. Compared with maintenance dialysis, most patients who receive a successful transplant experience an improved quality of life and a significant reduction in mortality. According to the Organ Procurement and Transplantation Network of the U.S. Health Resources and Services Administration, over 375,000 renal transplants have been performed in the United States since 1988. In 2014 alone, 17,108 renal transplants were performed, of which 11,570 were from deceased donors and 5,538 were from living donors. Unfortunately, there remains a huge imbalance between organ availability and demand. Although the number of candidates on the waiting list has increased, the total number of renal transplants performed in the United States has not increased significantly in the last decade. When a renal transplant is performed, every effort is made to address allograft dysfunction by management of immunosuppression and transplant complications. Five-year survival rates for the graft in renal transplant patients range from 72% to 99%, with the best rates seen in patients receiving kidneys from living donors.

Although the timing of intrinsic renal dysfunction may aid in narrowing the differential diagnosis, there is significant overlap between the various etiologies. In the immediate postoperative period (<1 week), the most common etiology of intrinsic dysfunction is acute tubular necrosis (ATN). ATN is seen in the immediate post-transplant period in a high percentage of cadaver grafts but occurs infrequently in living related donors. Acute rejection occurs from 1 week to 1 month after transplantation. Fortunately, acute rejection is an uncommon occurrence in current practice. Although the introduction of calcineurin inhibitors (cyclosporine and tacrolimus) has dramatically reduced the rate of acute allograft rejection, these drugs are nephrotoxic at supratherapeutic levels. Toxicity is most common in the second or third month after transplantation, when the drugs are being titrated. Chronic rejection is the most common cause of late graft dysfunction and presents at least 3 months following transplantation.

Like intrinsic renal dysfunction, vascular complications and peri-transplant collections are most often encountered during specific postoperative time periods. Renal artery thrombosis (RAT) and renal vein thrombosis (RVT) usually occur in the first week after transplantation. They are usually the result of technical surgical difficulties and/or clotting disorders. Renal artery stenosis (RAS) is the most common vascular complication, with an incidence of 1% to 2%. Although it can occur at any time, RAS usually presents between 3 months and 24 months following transplantation. Peri-graft collections occur in up to 50% of patients following transplantation. Seromas and hematomas generally occur in the first week following surgery. Abscesses and urinomas usually occur 1 to 3 weeks after transplantation. Lymphoceles typically present 1 to 2 months after transplantation.

Radiology plays a critical role in the diagnosis and management of renal transplant dysfunction. Ultrasound (US) is the modality of choice to evaluate renal transplants early in the postoperative period, in the post-transplant period, and also for long-term follow-up. US is also used to guide diagnostic and therapeutic interventions such as biopsy, nephrostomy placement, and fluid aspiration. Radionuclide imaging is a modality capable of assessing graft function both qualitatively and quantitatively. Computed tomography (CT) and magnetic resonance imaging (MRI) can provide information about structural abnormalities like arterial stenosis and arterial or venous thrombosis. Angiography is used for treatment of complications like RAS, pseudoaneurysm (PSA), and arteriovenous fistula (AVF).

Ultrasound

Since renal transplants typically are located anteriorly in the pelvis, they are usually readily examined with US. US is routinely used to evaluate the transplant within the first 24 hours after transplantation and also serves as the first-line evaluation method following the onset of transplant dysfunction. Grayscale images are obtained to evaluate for transplant size, echotexture, hydronephrosis, peri-transplant fluid collections, and masses and to measure renal cortical thickness. Color Doppler images evaluate the patency and direction of flow in transplant arteries and veins. Spectral analysis of vascular waveforms and velocities can provide information about a range of pathologies, including RAS and RVT. Advantages of US over CT include portability, no radiation exposure, and the lack of need for potentially nephrotoxic iodinated contrast agents. US is fast and real time, particularly when compared to MRI. Vascular evaluation with US instead of MRI can avoid the risk of nephrogenic systemic fibrosis (NSF) from gadolinium-based contrast agents. A relative limitation of US in comparison to CT or MRI is its operator dependence.

Grayscale US abnormalities in dysfunctional renal transplants include a reduction in corticomedullary differentiation, reduction in renal sinus echogenicity, increased and reduced renal parenchymal echoes, and increased cortical echogenicity. Unfortunately, these findings are of limited value as the features are nonspecific and generally occur well after the onset of transplant dysfunction.

Renal segmental or intralobar artery resistive indices (RI), measured by duplex Doppler US, are often used as a nonspecific parameter for allograft dysfunction. Although RI values differ between normal and abnormal allografts, studies have suggested that the RI is neither sensitive nor specific in identifying the cause of functional transplant dysfunction. Using $RI > 0.90$ in 145 examinations of 81 patients, one study found a sensitivity of 13%, a specificity of 100%, a positive predictive value (PPV) of 100%, and a negative predictive value (NPV) of 66% in making the diagnosis of acute rejection with duplex Doppler US. Another study found a sensitivity of 9%, a specificity of 91%, a PPV of 29%, and an NPV of 70% using an RI cutoff of 0.90 for the diagnosis of allograft rejection. Previous studies have shown that renal arterial RI is useful in predicting graft survival, especially when using a lower RI cutoff of 0.8. One research group, using a cutoff of 0.80 at 3 months after transplantation, found that 47% of patients with $RI > 0.80$ developed chronic allograft nephropathy (CAN), compared to 9% of patients with $RI < 0.80$. Another group found that both RI and pulsatility index measured between week 1 and 3 months significantly correlated with the 1-year estimated glomerular filtration rate.

Although an $RI > 0.80$ was initially thought to correlate with allograft dysfunction, a recent study raises doubt on this theory. This single-center prospective study analyzed RI at the time of protocol-specified renal allograft biopsies in addition to patients with graft dysfunction. Patients with $RI > 0.80$ did have 4.12 times higher mortality at 24 months than those < 0.80 , but their need for dialysis did not differ. The RI was significantly higher at the time of biopsy performed in patients with graft dysfunction, but changes in the RI did not reflect changes in histologic features when biopsies were performed at protocol-specific time points. The authors of the study surmised that these changes did not reflect an underlying intrarenal disease process but were related to patient age and central hemodynamic factors. This complex interaction of coexisting factors in renal transplants makes the interpretation of Doppler parameters difficult. Despite this recent study, US with Doppler imaging remains the first-line imaging in the early post-transplantation period as it establishes a baseline for future comparisons.

Doppler US is a first-line noninvasive tool in the evaluation of suspected RAS and uses a combination of direct insonation of the anastomosis and main renal artery in addition to indirect intrarenal waveform morphology. Peak systolic velocity (PSV) in the renal artery is commonly used as the parameter to assess for the presence of RAS on US. Cutoff values of 200 to 300 cm/s have been proposed in various studies, but the lower limit suffers from low specificity, leading to unnecessary angiography procedures. As in native kidneys, a tardus parvus waveform (small peak amplitude with delayed upstroke) can be seen within the transplanted kidney downstream to the stenosis. This morphologic waveform change is reflected quantitatively by the acceleration time (AT). One study reported a sensitivity of 90% to 96.8% and a specificity of 87.5% to 70% using various PSV thresholds in the main renal artery and a sensitivity of 100% and specificity of 96.7% using an AT of 0.09 or less as normal. Another parameter that can be used is the renal artery to iliac artery ratio, which has been shown to have a sensitivity of 90% and specificity of 96.7% using a cutoff value of 1.8. Alternatively, another study found that a PSV of 285 cm/s or renal-aortic ratio of 3.7 alone was better than any combination of PSVs, end-diastolic velocities, or renal-aortic ratios in detecting $\geq 60\%$ stenosis. As evaluation for RAS with US is operator dependent, MR angiography (MRA) or CT angiography (CTA) may be more reliable in centers with little experience in evaluating for RAS with US.

The US appearance of RAT is striking, with complete absence of flow in the renal vessels on color flow and spectral analysis. Power Doppler imaging may be helpful because of its capability to detect low flow. However, it is important to remember that the absence of arterial flow within the kidney can also be seen in patients with hyperacute rejection and RVT. Absence of renal venous flow and renal enlargement are classically seen in patients with RVT. Reversal of flow in the renal artery in diastole is often found in association with RVT; however, this represents only

approximately 10% of cases of reversed diastolic flow. Reversal of flow is seen more commonly in rejection or ATN and occasionally with nephrosclerosis.

US is also a useful tool in the detection of PSAs and AVFs, which may occur after biopsy. Although these complications resolve spontaneously in most cases, they can affect allograft function if they are large. PSAs may appear as a simple or minimally complex cyst on B-mode US. On color Doppler, a "yin-yang" flow pattern is usually seen within the body of the pseudoaneurysm. The spectral Doppler appearance of to-and-fro flow is detected in the neck of the pseudoaneurysm. Although often treated with endovascular technique, anatomically suitable PSAs can be treated with US-guided percutaneous thrombin injection. While often detectable on B-mode US, AVFs demonstrate a focal mosaic appearance on color Doppler secondary to tissue reverberation. On spectral Doppler, the feeding artery demonstrates a high-velocity, low-resistance waveform, and the draining vein waveform may be pulsatile or "arterialized."

Postoperative fluid collections like abscess, hematoma, lymphocele, and urinoma can be identified on US, but it cannot reliably differentiate between them. Sometimes an US examination may not demonstrate the extent of the collection and a noncontrast CT may be required. If large, these collections can lead to hydronephrosis; compression of the renal vein, leading to RVT; or compression of femoral vessels, leading to lower-extremity swelling or deep venous thrombosis. Large hematomas may lead to Page kidney. The time frame in which the collection is discovered has some prognostic ability since urinomas, hematomas, and abscesses occur in the early postoperative period, whereas lymphoceles occur weeks to months after surgery. Lymphoceles more often have septa than other collections, and hematomas tend to have higher echogenicity. In order to differentiate these entities, aspiration is usually required, and this is commonly performed with US guidance. Hydronephrosis can also be easily identified with US; however, it should be interpreted in correlation with biochemical data since reflux can give a similar appearance as well. Urine leak may appear as a fluid collection on US, but an isotope scan would be more helpful. Leaks are definitively diagnosed by aspiration of the collection with measurement of creatinine.

Since ATN and acute rejection cannot be diagnosed with US and serum creatinine is insensitive for detecting early graft pathology, US-guided biopsy is the standard method for the diagnosis of rejection and evaluation of immunosuppression. The complication rate from renal transplant biopsies is low, with a reported rate of 0.4% to 1% graft loss in approximately 2500 biopsies.

Contrast-enhanced US (CEUS) has been used by some investigators to evaluate graft perfusion both in large arteries and within the cortex. One research study found that patients with CAN had significantly lower blood flow values quantified by CEUS compared to patients without CAN. In a small series, CEUS was found to be helpful in differentiating the underlying causes of delayed graft dysfunction. CEUS can confirm transplant RAS and also aids in the assessment of the degree of stenosis. Currently, CEUS has not received approval by the U.S. Food and Drug Administration.

US-based elastography is another tool that may aid in the noninvasive assessment of CAN. The parenchymal stiffness measured by the transient elastography technique correlates with underlying histologic interstitial fibrosis. Unfortunately, kidney stiffness is not just related to the degree of fibrosis but is also related to functional and mechanical parameters. Although this new tool has promise, further validation is needed in clinical practice.

Computed Tomography and Computed Tomography Angiography

The utilization of CT of the abdomen and pelvis with contrast should be considered in conjunction with the risks of nephrotoxicity from iodinated contrast. It may be beneficial in evaluating renal masses, perinephric fluid collections, and post-transplant lymphoproliferative disease.

In patients with suspected vascular complications (RAS, RVT, PSA, AVF), CTA can provide a detailed anatomic depiction prior to undergoing percutaneous angiography. Data about the usefulness of CT in evaluating transplant vascular complications are limited. One study found abnormalities on CT in 42% of cases when US was unremarkable. These included renal infarction, renal vein stenosis, and AVF. Another study of native kidney vasculature found that CTA and MRA have comparable negative predictive accuracy in evaluating suspected RAS. They found that CTA had 94% sensitivity, 93% specificity, 71% PPV, and 99% NPV. A small series that compared CTA and MRA in the assessment of transplant RAS also demonstrated little difference between the modalities. CTA, however, has the drawback of potential postcontrast acute kidney injury and radiation exposure in addition to insensitivity to mild RAS.

A noncontrast CT of the abdomen and pelvis may be helpful in patients with suspected hemorrhage or in the evaluation for nephrolithiasis in the transplant kidney. It also may be useful to define the extent of a peritransplant fluid collection or in patients who cannot receive intravenous contrast.

Magnetic Resonance Imaging and Magnetic Resonance Angiography

MRI is being increasingly used as a second-line imaging modality for the evaluation of kidney transplants. Like a CT with and without contrast, an MRI with and without contrast may aid in characterization of renal masses and perinephric fluid collections. Although the risk of nephrotoxicity

following gadolinium chelate contrast administration remains controversial, there is increased risk for NSF in this patient population that often has compromised renal function. Fortunately, nonenhanced MRI pulse sequences may provide useful information in patients that have contrast contraindications and serve as an alternative to CT.

Although digital subtraction angiography remains the reference standard for the anatomic delineation of the renal arteries, MRA permits a noninvasive method to evaluate for RAS and does not expose the patient to ionizing radiation. Although MRA protocols may not provide the same parenchymal anatomic detail as a conventional MRI, MRA plays a critical role in the management of patients with transplant dysfunction. One study found that MRA resulted in a change in the referring clinician's initial diagnostic impression in approximately 65% of patients. In 35% of patients, angiography was avoided. Another group studied both native and transplant renal arteries and found that preprocedural planning with the use of gadolinium-enhanced MRA significantly reduced the iodinated contrast material requirement during percutaneous renal artery interventions, in addition to shortening the procedure duration. In studies evaluating the efficacy for native kidney RAS, one group found that MRA had a sensitivity of 90%, a specificity of 94%, a PPV of 75%, and an NPV of 98%. A similar study reported a sensitivity of 97%, a specificity of 67%, a PPV of 90%, and an NPV of 86% for diagnosing native RAS.

Unfortunately, MRA suffers from a few pitfalls that may lead to a false diagnosis of stenosis or an overestimation of a stenosis. These include artifacts caused by metallic surgical clips near the transplant artery that result in signal loss near the artery, giving the false impression of stenosis. Venous contamination due to inaccurate timing of the arterial bolus is another artifact that can affect the accuracy of diagnosis. Careful evaluation of the source images and multiplanar reformats will help solve these problems. In addition to depicting areas of stenosis in the main renal artery, MRA is able to depict areas of infarction within the kidney, which are seen as areas of heterogeneous T1 and T2 signal intensity and as focal areas of nonenhancement on the postcontrast images. Using 3D gadolinium-enhanced MRA for the detection of transplant RAS, one research group showed a sensitivity of 93.7%, a specificity of 80%, and an accuracy of 88.5%. In addition, outer cortical necrosis, cortical necrosis with large patches, diffuse cortical necrosis, and both cortical and medullary necrosis were visualized. The loss of corticomedullary differentiation has been described in post-transplant patients with cyclosporine toxicity, rejection, and ATN.

Noncontrast MRA (NC-MRA) with steady-state free precession imaging can help avoid contrast utilization and avoid the risk of NSF. Several studies have evaluated the value of NC-MRA in the evaluation of native RAS. In these studies, NC-MRA of renal arteries demonstrated a sensitivity of 78% to 100%, a specificity of 82% to 99%, and an NPV of 95% to 100% in the detection of significant arterial stenosis (>50%). The PPV (57% to 92%) was lower than other parameters. The high NPV suggests that NC-MRA can be used as a screening tool for detecting RAS. When positive, other imaging modalities can be utilized for confirmation and to better assess the degree of stenosis. Although technically more challenging and requiring a longer examination time, 2 small studies suggested that NC-MRA was capable of detecting transplant RAS with a similar accuracy to gadolinium-enhanced MRA.

Newer MRI techniques such as diffusion-weighted MRI (DWI-MRI) and blood oxygen level-dependent (BOLD) imaging have shown considerable promise as noninvasive techniques to detect functional changes in kidneys. BOLD imaging depends on contrast generated by changing levels of paramagnetic deoxyhemoglobin with a decrease in intrarenal T2 signal during hypoxia, taken as a reflection of increasing concentrations of deoxyhemoglobin. BOLD imaging can noninvasively detect changes in intrarenal oxygenation. This technique may be useful in the differentiation of acute rejection from ATN and to identify the hypoxia induced by RAS. DWI-MRI is based on the thermally induced Brownian motion of water molecules in tissue. The quantitative apparent diffusion coefficient derived from this sequence provides information on the diffusion properties of the tissue evaluated. This technique has demonstrated promise as an indicator of allograft dysfunction. A recent study suggests that although these techniques may prove useful in the assessment of function, they are limited in the characterization of the underlying cause. The addition of diffusion tensor imaging to DWI may increase the sensitivity in detecting pathologic changes in renal transplants. Further investigation is needed to validate the diagnostic value of these techniques in detecting allograft dysfunction.

X-ray Intravenous Urography and Pyelography

X-ray intravenous urography and pyelography are no longer used for evaluation of the renal transplant.

Nuclear Medicine

Radionuclide tests are valuable in renal transplantation since they provide a noninvasive means to evaluate transplant function qualitatively and also screen for surgical complications. Only scintigraphic studies are able to separate function of the graft from residual function of the native kidneys or any remaining prior failed graft. Renal scintigraphy assesses the 3 sequential phases of renal function. For the first minute following tracer injection, rapid dynamic imaging evaluates perfusion. The nephrons extract the tracer from the blood and excrete it by glomerular filtration and/or tubular secretion in the second phase. In the third phase, the tracer drainage allows assessment of urinary flow.

Although the use of radionuclide renal imaging during the early post-transplantation period has decreased, there are still centers that routinely perform them prior to patient discharge from the hospital to serve as a baseline study for future comparison. An advantage of renography is that it provides functional information, whereas blood creatinine levels lag behind function and radiographic studies are primarily anatomic. Because of

this, it can be helpful in evaluating the return of function after ATN or rejection.

One research group found scintigraphy performed within 2 days of transplantation was superior to RI in predicting long-term graft function. Another group found that a renogram performed 1 to 2 days after transplantation could predict primary graft nonfunction, prolonged time to graft function, low hospital discharge chromium ethylenediaminetetraacetic acid (EDTA) clearance, and low 1- and 5-year graft survival, whereas a renogram performed at discharge could predict late (>6 months) graft loss.

Although sensitive in the detection of graft dysfunction, scintigraphic parameters do not yield sufficient diagnostic power for a specific diagnosis. Like RI, renogram changes do not contribute to the differential diagnosis between acute rejection, ATN, and cyclosporine toxicity.

RAS appears similar to the scintigraphic findings seen with rejection. Angiotensin-converting enzyme inhibitor renography can aid in the diagnosis if baseline studies are available for comparison. In obstruction, scintigraphy can be used in conjunction with furosemide, as it is in native kidneys. Urinary leaks can be identified by the presence of radioactivity in an abnormal location. In some centers and especially in Europe, renal clearances are performed serially to evaluate renal function. These are performed less frequently in the United States.

Numerous quantitative indexes are used to evaluate transplants. Although no single parameter has achieved acceptance, it appears that they may be useful. Tc-99m diethylenetriamine pentaacetic acid (DTPA) or Tc-99m mercaptoacetyltriglycine (MAG3) can be used to follow the transplant. Because of its higher extraction fraction and better image quality, MAG3 is preferred at most transplant centers. DTPA, which is not excreted, is limited in the evaluation for obstruction, only demonstrating early impact on glomerular filtration. In a limited number of studies, MAG3 has not been proven superior to DTPA.

Angiography

RAS is reported to occur in 1% to 23% of patients following transplantation and accounts for 1% to 5% of renal transplant hypertension. Percutaneous therapeutic angioplasty (PTA) and stenting (PTAS) is the treatment of choice for RAS, with a success rate of 65% to 100%. The complication rate from PTA and PTAS of 0% to 10% is low compared to surgery, which has a graft loss rate of 15% and mortality rate of 5%. However, in 1 long-term study over a 24-year period, the researchers found a higher complication rate of 25.5% (usually without clinical sequelae). The majority of these complications were related to arterial access.

In a study of 44 patients, the technical success rate of PTA was 100% and the 5-year graft survival rate was 86%. The restenosis rate after PTA has been reported to be between 10% and 56%. Another study found a technical success rate of 100% with no acute complications, amelioration of arterial hypertension, and improvement of graft function within 7 postoperative days following PTAS. In the follow-up period, 81.8% of patients had normal blood pressure and creatinine levels, suggesting that PTA was effective. PTAS restenosis rates are even lower than PTA at between 5% and 30%. Studies comparing PTA and PTAS are sparse. Although off-label utilization of drug-eluting stents has been used to treat RAS, larger studies are needed to prove them advantageous over bare metal stents.

The treatment of PSAs is indicated if the patient is symptomatic, the aneurysm diameter is >2.5 cm, expansion is noted on repeat imaging, or the etiology is infectious. Endovascular treatment is performed with coil embolization or stent grafting.

AVFs are almost always iatrogenic, usually occurring following a graft biopsy. Although most resolve spontaneously, superselective embolization is highly effective, with minimal loss of renal parenchyma when needed.

Summary of Recommendations
















- US duplex Doppler is the first-line imaging evaluation method to assess the presence and causes of renal transplant dysfunction.
- Renal scintigraphy using MAG3 serves a complementary role by quantitatively assessing the 3 sequential phases of renal transplant function.
- Although US, CTA, and MRA can noninvasively diagnose RAS, angiography remains the diagnostic reference standard and is utilized to guide intervention.

Abbreviations

- CT, computed tomography
- CTA, computed tomography angiography
- DTPA, diethylenetriamine pentaacetic acid
- IV, intravenous
- MAG3, mercaptoacetyltriglycine
- MRA, magnetic resonance angiography
- MRI, magnetic resonance imaging
- RAS, renal artery stenosis

- Tc-99m, technetium 99 metastable
- US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
	<0.1 mSv	<0.03 mSv
 	0.1-1 mSv	0.03-0.3 mSv
  	1-10 mSv	0.3-3 mSv
   	10-30 mSv	3-10 mSv
    	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Renal transplant dysfunction, including transplant rejection, acute tubular necrosis, renal artery and renal vein thrombosis, renal artery stenosis, pseudoaneurysm, and arteriovenous fistula

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Critical Care

Family Practice

Internal Medicine

Nephrology

Nuclear Medicine

Radiology

Surgery

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging procedures for patients with renal transplant dysfunction

Target Population

Patients with renal transplant dysfunction

Interventions and Practices Considered

1. Ultrasound (US) duplex Doppler, kidney transplant
2. Technetium (Tc)-99m mercaptoacetyltriglycine (MAG3) scan, kidney
3. Tc-99m diethylenetriamine pentaacetic acid (DTPA) scan, kidney
4. Computed tomography (CT), abdomen and pelvis
 - With intravenous (IV) contrast
 - Without and with IV contrast
 - Without IV contrast
5. Arteriography, kidney
6. CT angiography, abdomen and pelvis, with IV contrast
7. Magnetic resonance imaging (MRI), abdomen and pelvis
 - Without and with IV contrast
 - Without IV contrast
8. Magnetic resonance angiography (MRA), abdomen and pelvis
 - Without and with IV contrast
 - Without IV contrast
9. X-ray
 - IV urography
 - Antegrade pyelography

Major Outcomes Considered

Accuracy, sensitivity, specificity, and positive and negative predictive value of imaging procedures for evaluating renal transplant dysfunction

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 90 citations in the original bibliography, 47 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in May 2015 and updated December 2015 to identify additional evidence published since the *ACR Appropriateness Criteria® AC Renal Transplant Dysfunction* topic was finalized. Using the search strategy described in the literature search companion (see the "Availability of Companion Documents" field) 16,408 articles were found. Thirty-eight articles were added to the bibliography. The remaining articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased.

The author added 4 citations from bibliographies, Web sites, or books that were not found in the new literature search.

One citation is a supporting document that was added by staff.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 90 citations in the original bibliography, 47 were retained in the final document. The new literature search conducted in May 2015 and updated in December 2015 identified 38 articles that were added to the bibliography. The author added 4 citations from bibliographies, Web sites, or books that were not found in the new literature search. One citation is a supporting document that was added by staff.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);

Or

The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;

Or

The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness. When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the second rating round, the recommendation is "May be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the [Rating Round Information](#) document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the [ACR Web site](#) (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 90 references cited in the *ACR Appropriateness Criteria® Renal Transplant Dysfunction* document, 67 are categorized as diagnostic references, including 2 well-designed studies, 23 good-quality studies, and 21 quality studies that may have design limitations. Additionally, 23 references are categorized as therapeutic references, including 15 good-quality studies and 1 quality study that may have design limitations. There are 28 references that may not be useful as primary evidence.

Although there are references that report on studies with design limitations, 40 well-designed or good-quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Radiology plays a critical role in the diagnosis and management of renal transplant dysfunction. Ultrasound (US) is the modality of choice to evaluate renal transplants early in the postoperative period, in the post-transplant period, and also for long-term follow-up. US is also used to guide diagnostic and therapeutic interventions, such as biopsy, nephrostomy placement, and fluid aspiration. Radionuclide imaging is a modality capable of assessing graft function both qualitatively and quantitatively. Computed tomography (CT) and magnetic resonance imaging (MRI) can provide information about structural abnormalities like arterial stenosis and arterial or venous thrombosis. Angiography is used for treatment of complications like renal artery stenosis (RAS), pseudoaneurysm (PSA), and arteriovenous fistula (AVF).

Potential Harms

- The utilization of computed tomography (CT) of the abdomen and pelvis with contrast should be considered in conjunction with the risks of

nephrotoxicity from iodinated contrast.

- Magnetic resonance angiography (MRA) suffers from a few pitfalls that may lead to false diagnosis of stenosis or overestimation of a stenosis. These include artifacts caused by metallic surgical clips near the transplant artery that result in signal loss near the artery, giving the false impression of stenosis. Venous contamination due to inaccurate timing of the arterial bolus is another artifact that can affect the accuracy of diagnosis.
- Although the risk of nephrotoxicity following gadolinium chelate contrast administration remains controversial, there is increased risk for nephrogenic systemic fibrosis (NSF) in patients with kidney transplants, who often have compromised renal function.
- Ultrasound (US)-guided biopsy is the standard method for the diagnosis of rejection and evaluation of immunosuppression. The complication rate from renal transplant biopsies is low, with a reported rate of 0.4% to 1% graft loss in approximately 2500 biopsies.
- The complication rate from percutaneous therapeutic angioplasty (PTA) and stenting (PTAS) of 0% to 10% is low compared to surgery, which has a graft loss rate of 15% and mortality rate of 5%. However, in 1 long-term study over a 24-year period, the authors found a higher complication rate of 25.5% (usually without clinical sequelae). The majority of these complications were related to arterial access.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Taffel MT, Nikolaidis P, Beland MD, Blaufox MD, Dogra VS, Goldfarb S, Gore JL, Harvin HJ, Heilbrun ME, Heller MT, Khatri G, Preminger GM, Purysko AS, Smith AD, Wang ZJ, Weinfeld RM, Wong-You-Cheong JJ, Remer EM, Lockhart ME, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® renal transplant dysfunction. Reston (VA): American College of Radiology (ACR); 2016. 12 p. [90 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

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Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Urologic Imaging

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dighe M, Remer E, Casalino D, Bishoff JT, Blaufox MD, Coursey CA, Eberhardt SC, Goldfarb S, Harvin HJ, Lazarus E, Leyendecker JR, Lockhart ME, Nikolaidis P, Oto A, Porter C, Sheth S, Vikram R, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® renal transplant dysfunction. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 7 p. [55 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [American College of Radiology \(ACR\) Web site](#) .

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the [American College of Radiology \(ACR\) Web site](#) .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2016. 4 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2016. 128 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2016 May. 2 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria® renal transplant dysfunction. Evidence table. Reston (VA): American College of Radiology; 2016. 38 p. Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria® renal transplant dysfunction. Literature search. Reston (VA): American College of Radiology; 2016. 2 p. Available from the [ACR Web site](#) .

Patient Resources

None available

NGC Status

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